International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Psychological Impact of Tuberculosis and Anti-Tuberculosis Drugs: A Longitudinal Study of Emotional Symptoms Among Tuberculosis Patients

Abderrahmane Boualam[1], Amine Rkhaila[2], Mouhatti Saga[2], Noufissa Kouddane[1], Nabyl Berrid[1], El Mahjoub Aouane[1]*

[1]*Laboratory of Natural Resources and Sustainable Development, Department of Biology, Faculty of Sciences, Ibn-Tofail University, Kenitra, Morocco.*

[2]*Plant, Animal and Agro-Industry Productions Laboratory, Department of Biology, Faculty of Sciences, University Campus, Ibn Tofail University, Kenitra, Morocco.*

Abstract

Tuberculosis (TB) is a highly infectious disease, primarily caused by *Mycobacterium tuberculosis*. This study aimed to assess the psychological effects on patients undergoing treatment at the TB and respiratory disease diagnostic facility in Sidi Kacem-Morocco Province. Furthermore, research has endeavored to identify patients' specific psychosocial support needs. The study presents data from a thorough three-year investigation (2018-2020) that shows a significant occurrence of psychiatric symptoms among patients with tuberculosis. For instance, many patients in 2020 reported experiencing exhaustion, with 55.74% of females and 61.24% of males reporting persistent fatigue. In 2020, a significant number of individuals reported experiencing persistent anxiety, with over 40% of men and 44% of women being affected. The prevalence of chronic stress was also a cause of concern, with 34% of men and 37% of women experiencing this condition. Similarly, a substantial proportion of the population reported feelings of sadness and despair. In 2020, 45% of the men and 51% of the women reported experiencing persistent sadness. In the same year, a sizeable proportion of individuals, specifically 31% of men and 45% of women, experienced an ongoing condition of despair, characterized by a continuous and pervasive feeling of hopelessness. Persistent feelings of worthlessness were prevalent among a significant proportion of individuals (72% of men and 74% of women) who consistently reported experiencing such feelings throughout 2018. The abbreviations of the technical terms are explained upon their initial usage. Grammatical correctness and adherence to language and formatting conventions ensured a clear comprehension of the findings. These symptoms persist throughout therapy, particularly in relation to the impact of anti-TB drugs on mental well-being, with minimal fluctuations from year to year. The citation and footnote styles conform to the standardized guidelines. Biased or subjective evaluations are avoided, and clear objective wording is employed throughout, utilizing high-level language and precise vocabulary specific to the subject matter. It is important to recognize that the COVID-19 pandemic has had a distinct impact on the psychological distress experienced by individuals with tuberculosis (TB), further intensifying their stress and anxiety levels.

Keywords: Tuberculosis, anti-tuberculosis medication, psychological impact, psychosocial impact

Full-length article **Corresponding Author*, e-mail: amine.rkhaila@uit.ac.ma

1. Introduction

Tuberculosis is a very consequential pulmonary bacterial disease that has been well acknowledged for its serious detrimental effects on physical well-being. Nevertheless, the scientific community has often neglected to consider the psychological impacts. Furthermore, due to the increasing prevalence of individuals experiencing psychological repercussions from this health issue, the scientific community has initiated extensive research to enhance comprehension of the psychological impact of this disease, which is commonly regarded as primarily physical [1]. In light of this consideration, global surveys have undertaken investigations into various facets of the interplay between tuberculosis (TB) and mental health. One notable study conducted in the United States by Redford and Mayer-Barber [2] delved into the realm of psychiatric comorbidities linked to TB, thereby underscoring the paramount significance of holistic patient management. Furthermore, a multicenter survey spanning Southeast Asia, spearheaded by Pachi et al. [3], was instrumental in evaluating the mental well-being of TB patients across multiple nations. This

comprehensive inquiry unveiled the prevalence of psychiatric disorders within this patient cohort and accentuated the pivotal role of mental health in fostering treatment adherence and post-treatment monitoring.

Moreover, the psychological ramifications of anti-tuberculosis medications found scrutiny in a Belgian investigation carried out by Andries et al. [4]. This inquiry shed light on the psychiatric symptoms associated with the administration of isoniazid, one of the most frequently prescribed anti-tuberculosis drugs. These studies collectively contribute to our understanding of the intricate relationship between TB and mental health, emphasizing the necessity for a holistic approach to patient care that addresses both the physical and psychological dimensions of this debilitating disease. This study aims to evaluate over three consecutive years (2018-2019-2020) the impact of tuberculosis and anti-tuberculosis drugs on the mental health of tuberculosis patients cared for at the tuberculosis and respiratory disease diagnostic center in the province of Sidi Kacem-Morocco, and to identify psychosocial support needs to improve their psychological well-being throughout their treatment.

2. Materials and methods

2.1. Study site

Diagnostic center for tuberculosis and respiratory diseases (CDTMR) in the province of Sidi Kacem-Morocco.

2.2. Sample

Our sample included 600 male and female patients, aged between 1 and 65 years or older, diagnosed with tuberculosis.

2.3. Inclusion and exclusion criteria

All patients with an age between 1 and 65 or more, managed in tuberculosis and respiratory diseases diagnostic center in Sidi Kacem province during the years 2018-2019-2020.

2.4. Study instrument

A structured questionnaire was developed to collect data by reviewing a large number of relevant research papers and consulting experts in related fields [5]. Prior to the actual data collection, the questionnaire was translated into Arabic and adapted to the Moroccan context. We then conducted a pre-survey in the research establishment. Based on feedback, the questionnaire was modified and completed to ensure its effectiveness. Psychological distress was assessed using the Kessler Psychological Distress Scale (K-10) [6]. The scale was a 10-item self-report tool used to measure non-specific symptoms of depression and anxiety [7]. Participants' responses to each item were scored on a Likert scale ranging from 1 (never) to 5 (all the time). The total score was the sum of the scores for each item, on a scale from 10 to 50. The higher the score, the greater the degree of psychological distress. Those whose scores were equal to or higher than 16 were considered to be suffering from psychological distress [6]. In this study, Cronbach's α was 0.929.

2.5. Ethical aspects

Authorization for data collection was sought from the Dean of the Faculty of Science covering the period of the study. Initially, this authorization was presented to the Delegation of Health within the province of Sidi Kacem for a favorable opinion.

2.6. Statistical analysis

The data collected were entered into Excel, then transferred to another statistical software package for analysis of variance using the one-factor ANOVA test.

3. Results and discussion

Analysis of the incidence of fatigue among TB patients is essential for understanding the mental health implications of TB. The survey findings indicate that weariness is a commonly seen symptom among those diagnosed with tuberculosis. The lack of surprise about this discovery may be attributed to the inherent characteristics of the disease and its significant consequences on the immune systems and overall well-being of affected individuals. It is noteworthy to mention that a majority of the participants in this research reported experiencing persistent or regular exhaustion, indicating the substantial influence of tuberculosis on their levels of energy and vitality. The chronic fatigue experienced by individuals may significantly impede their everyday functioning and possibly have a negative impact on their overall well-being (Table 1). The findings indicate a higher likelihood of women reporting chronic fatigue compared to males. The prevalence of response rates indicating "persistent" or "regular" weariness is much greater among females compared to males. These reports exhibit a lack of bias. This finding may be attributed to biological reasons or socio-cultural elements. This research emphasizes the significance of considering gender in the management and treatment of TB. Fatigue is a significant symptom experienced by individuals with tuberculosis (TB), which has a profound impact on their ability to adhere to treatment and maintain a healthy lifestyle. Hence, it is essential to include fatigue reduction measures into the holistic therapy of tuberculosis patients in order to enhance their overall well-being. This may include the adoption of treatments focused on nutrition, the provision of psychological support, and the use of ways to efficiently manage everyday weariness. In general, the findings of the study emphasize the need of acknowledging and addressing tiredness among individuals diagnosed with tuberculosis (TB), while also considering the influence of gender differences in the treatment and control of the illness. The findings shown in Table 2 pertaining to the participants' experience of anxiousness for the years 2018, 2019, and 2020 provide valuable insights into the psychological consequences of this condition on the selected sample. It is noteworthy to acknowledge that a significant proportion of persons diagnosed with tuberculosis (TB) report experiencing varying levels of discomfort, indicating the prevalence of this issue among TB patients. Undoubtedly, a significant segment of the participants, especially the male respondents, have indicated the occurrence of uneasiness to varying degrees. Specifically, the prevalence of feeling nervousness "a little" has shown an upward trend, with percentages of 15% in 2018, 22% in 2019, and 40% in 2020. Similarly, the proportion of individuals reporting discomfort "most" of the time remained relatively stable, with figures of 37% in both 2018 and 2019, followed by a decrease to 22% in 2020. Furthermore, a major portion of respondents, including 41% in 2018, 36% in 2019, and 38% in 2020,

consistently reported having nervousness "all the time." This phenomenon underscores the psychological impact of tuberculosis, which may lead to heightened levels of stress and anxiety (Table 2).

Moreover, it is noteworthy to observe that women have a greater propensity towards experiencing feelings of nervousness compared to males, especially over the time period spanning 2019 and 2020. The sense of uneasiness may exhibit a gender gap, which may be attributed to several causes such as psychological reactions to disease and hormonal variations. When formulating psychological support techniques for individuals with tuberculosis, it is important to consider the influence of gender variance. When considering temporal fluctuations, it can be shown that rates of anxiousness exhibit minor oscillations on an annual basis, although exhibit a general trend of stability. This implies that individuals diagnosed with tuberculosis have persistent anxiety throughout the duration of their treatment, irrespective of prospective advancements in medical interventions. The findings of this study underscore the critical significance of providing psychological support to those diagnosed with tuberculosis, specifically emphasizing the treatment of stress and uneasiness. The provision of psychological support is of paramount importance in enhancing patient well-being and promoting adherence to treatment protocols. Furthermore, the acknowledgment of gender disparities in the reactions to feelings of anxiety emphasizes the need of providing distinct ways of assistance for individuals of various genders. The examination of data obtained from tuberculosis (TB) patients throughout the years 2018 (males n = 13, females n = 10), 2019 (males n = 13, females n = 17), and 2020 (males n = 5, females n = 2) relative to their stress levels and capacity to alleviate stress provides noteworthy observations on the psychological anguish experienced by this specific group (Table 3).

First and foremost, it is crucial to acknowledge that stress emerges as a prevalent issue among individuals diagnosed with tuberculosis (TB), as shown by significant proportions of patients reporting experiencing varying degrees of stress. A considerable proportion of male and female respondents have reported experiencing varying levels of stress, categorized as "a little," "most," or "all the time." The data from 2018, 2019, and 2020 indicate that the percentages of males and females falling into these categories have fluctuated. In 2018, the percentages for "a little" were 26% for males and 34% for females, while in 2019, they were 26% for males and 20% for females. In 2020, the percentages decreased to 24% for males and 20% for females. For the category of "most," the percentages in 2018 were 19% for males and 14% for females, which increased to 31% for males and 40% for females in 2019. In 2020, the percentages further increased to 34% for males and 37% for females. Lastly, for the category of "all the time," the percentages in 2018 were 13% for males and 15% for females, which increased to 19% for males and 13% for females in 2019. In 2020, the percentages further increased to 27% for males and 34% for females. The aforementioned results underscore the psychological burden associated with tuberculosis (TB), which has the potential to result in elevated levels of stress and anxiety. Moreover, it is noteworthy that women have a higher propensity for experiencing stress compared to males, notably during the years 2018 (M = 17, F = 10) and 2019 (M = 13, F = 17). The observed discrepancy in stress perception across genders might potentially be attributed to a range of causes, including psychological reactions to disease as well as biological variances. When developing psychological support programs for individuals with tuberculosis (TB), it is important to consider the influence of gender variance.

In relation to temporal fluctuations, it can be seen that stress rates exhibit modest year-to-year changes, however overall stability is maintained. This implies that stress continues to be a persistent issue for individuals with tuberculosis (TB) throughout the duration of their treatment, despite potential advancements in medicinal interventions. It is imperative to note that the feeling of hopelessness is a prevalent emotion among TB patients, as evidenced by the considerable percentages of respondents reporting feeling various degrees of hopelessness. A substantial proportion of patients, both male and female, report an experience of hopelessness, described as "a little", "most" or "all the time". In 2018, 36% of men and 28% of women expressed a feeling of hopelessness "all the time". In 2019, these proportions stood at 24% for men and 35% for women, while in 2020 they reached 42% and 44% respectively (Table 4). Furthermore, women appear to be more predisposed to feeling hopeless than men in all three years examined. In 2018, 41% of women reported feeling hopeless "most" of the time, compared with 28% of men. In 2019, this disparity continued, with 24% of women and 33% of men reporting an experience of hopelessness "most" of the time. In 2020, these figures rose to 45% for women and 31% for men. These findings highlight the significant psychological burden associated with tuberculosis, a potentially disabling disease, and underscore the imperative of tailored psychosocial care to address this component of the disease burden. The gender gap in the perception of hopelessness invites consideration of specific interventions aimed at improving patients' mental health and well-being throughout their fight against TB. Moreover, it is worth noting that TB patients often experience emotional states characterized by agitation or irritation, as shown by the substantial proportions of survey participants who reported experiencing these feelings to varied extents. A significant percentage of patients, regardless of gender, indicate the presence of agitation or irritability at varying frequencies, ranging from "occasionally" to "frequently" or "constantly" (Table 5). In the year 2018, a notable observation was made about the prevalence of agitation or irritability among patients. Specifically, it was found that 35% of male patients and 32% of female patients reported feeling these symptoms persistently, denoted as "all the time". The aforementioned pattern persisted throughout the year 2019, as shown by a survey in which 31% of men and 45% of women reported experiencing a persistent feeling of agitation or irritation. In the year 2020, the aforementioned percentages exhibited a sustained elevation, with figures of 45% and 51% seen for males and females, respectively. It is important to acknowledge that these findings need interpretation within the framework of the COVID-19 epidemic that transpired

during this timeframe. The global epidemic has resulted in elevated levels of worry, anxiety, and uncertainty among the general population, potentially influencing the emotional well-being of those diagnosed with tuberculosis. The concurrent presence of TB, a disease that already imposes significant physical and psychological burdens, with the COVID-19 pandemic, may have intensified the mental misery experienced by these individuals. Furthermore, it is noteworthy to observe that women have a greater propensity for experiencing agitation or irritability compared to males for the duration of the three-year period under investigation. The observed gender differential in this context might potentially be attributed to a range of reasons, including psychological reactions to disease as well as variances in hormone profiles. Considering gender diversity is of utmost importance when developing psychological support programs for individuals with tuberculosis (TB), especially within the framework of the COVID-19 pandemic.

Based on the statistics from 2018, a significant proportion of males (57%) and females (58%) had challenges in successfully doing their routine activities. The aforementioned pattern persisted over the years 2019 and 2020, with comparable proportions. Significantly, female participants indicated a higher prevalence of challenges compared to their male counterparts. In the year 2018, a considerable percentage of women, above 70%, reported encountering regular challenges in executing these jobs, with the qualifiers "most" or "all the time". In comparison, a somewhat lower proportion of male respondents, namely 57%, reported experiencing comparable challenges. The potential discrepancy in perceived challenges experienced by individuals of different genders may be impacted by several factors, such as psychological responses to sickness and differences in disease treatment approaches that are correlated with gender (see Table 6). The prevalence rates of patients encountering difficulties exhibit a degree of consistency over an extended duration. This implies that individuals afflicted with TB have persistent challenges in executing their customary activities throughout the course of their therapy. These findings underscore the substantial impact of TB on individuals' overall quality of life, specifically in terms of their capacity to engage in routine activities and fulfill their daily obligations. The challenges discussed may arise from the symptoms of diseases, bad responses to medications, or limits connected with treatment approaches. The comprehensive management of tuberculosis (TB) patients necessitates the incorporation of several components, including the delivery of medical interventions as well as the provision of psychological and emotional assistance with the objective of enhancing their overall welfare and enhancing their standard of living during their battle against TB. Throughout the duration of 2018, a significant observation was made pertaining to the emotional well-being of participants, specifically in relation to experiences of melancholy. The study revealed that a significant proportion of both males and females, namely 61% of males and 62% of females, indicated the occurrence of emotions of sorrow throughout a spectrum of intensities, ranging from mild to persistent. The aforementioned trend has shown a significant level of consistency during the preceding years, as seen by the data presented in Table 7. It is well acknowledged that women, as a demographic cohort, have a higher inclination to report instances of depression compared to males. In the year 2018, a higher percentage of females (75%) as compared to males (61%) indicated experiencing feelings of sadness. The discrepancy in the expression of melancholy across genders may be explained by several reasons, such as unique emotional coping mechanisms and divergent responses to physical and mental distress. There seems to be a minor fluctuation in the incidence of sorrow among patients during the duration of their medication, with some variation seen from year to year. It is noteworthy that a considerable proportion of individuals continually expressed notable degrees of melancholy throughout the duration of the research. This finding underscores the significant impact of TB on the psychological welfare of people. The emotional states of despair and helplessness might be exacerbated by the intrinsic qualities of the illness, including the difficulties linked to therapeutic interventions and the adverse impacts of pharmaceutical substances. In the context of providing comprehensive care for those diagnosed with TB, it is imperative to recognize the significance of including psychological therapy as an important component of their treatment regimen. The purpose of this component is to provide assistance in several domains, including emotional, psychological, and social dimensions. Consequently, it is anticipated that people would see enhancements not only in their quality of life but also in their mental well-being.

The examination of the data reveals that in the year 2018, a considerable percentage of both males (72%) and females (74%) reported experiencing feelings of devaluation. These emotions were reported to range in severity from "a little" to "all the time". This pattern persisted in the following years, with comparable proportions. In contrast, it is more probable for women to express comparable feelings compared to males. Based on the data from 2018, it was observed that a greater proportion of women (74%) reported experiencing a sense of worthlessness in comparison to males (72%). Several factors may contribute to the observed disparity in gender, such as psychological responses to disease, cultural norms and expectations, and variations in how society obligations and responsibilities are assessed (Table 8). Based on the data from 2018, it was observed that a greater percentage of women (74%) compared to males (72%) reported experiencing a sense of devaluation. In the year 2018, a greater percentage of women (74%) as compared to males (72%) indicated experiencing a sense of devaluation. The data indicates that there has been little variation in the percentages of persons who report experiencing emotions of inadequacy over a prolonged duration. This discovery indicates that a significant number of patients undergoing tuberculosis treatment have persistent thoughts of insignificance.

The research listed above emphasize the considerable influence of tuberculosis (TB) on the psychological well-being of people, specifically in relation to self-perception and emotions of value. The experience of negative emotions may possibly emerge due to the restrictions imposed by the illness, unfavorable effects of medication, and physical limits. The incorporation of a psychosocial support element is crucial in the comprehensive care of individuals diagnosed with TB, with a particular emphasis on their psychological and emotional welfare. The research conducted by Tola et al. [8]

demonstrated a noteworthy correlation between two variables and the anticipation of psychological distress. Specifically, the diagnosis of multidrug-resistant tuberculosis and a precarious economic situation were found to be significantly associated with psychological distress after a six-month period subsequent to the initiation of anti-tuberculosis treatment. Furthermore, this research study has successfully found three elements that are significantly correlated with treatment result. These factors include the patient's previous experience with antituberculosis therapy, their employment position, and the existence of psychological distress symptoms six months into the treatment process.

Table 1: Percentage of the obtained responses from TB patients who received treatment at the medical facility about their subjective experience of weariness

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long do you feel tired for no apparent reason?	Not at all	12 a	09 a	14 a	03 a	01 a	02 a
	Very little	10 a	13 ab	20 ab	14 b	04 a	05 a
	Somewhat	26 b	19 b	16 a	12 b	06 a	05 a
	Most of the time	38 c	31 c	35 c	41 c	45 b	38 b
	All the time	14 a	28 c	15 a	30 c	44 b	50 c
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 2: Percentage of patients with TB reported anxiousness

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long do you feel nervous?	Not at all	02 a	00 a	04 a	02 a	00 a	00 a
	Very little	05 a	02 b	01 a	01 a	00 a	00 a
	Somewhat	15 b	23 c	22 b	26 b	40 c	42 c
	Most of the time	37 c	42 d	37 c	34 b	22 b	19 b
	All the time	41 c	33 cd	36 c	37 b	38 c	39 c
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level.

Table 3: Percentage of Tuberculosis Patients' Perceived Stress Levels

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long have you felt so stressed that nothing calmed you down??	Not at all	18 a	17 a	13 a	10 a	05 a	02 a
	Very little	24 b	20 a	11 a	17 a	10 a	07 a
	Somewhat	26 b	34 b	26 b	20 a	24 b	20 b
	Most of the time	19 a	14 a	31 b	40 b	34 b	37 c
	All the time	13 a	15 a	19 a	13 a	27 b	34 c
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 4: TB patients' responses to feelings of hopelessness

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F

How long have you felt desperate?	Not at all	07 a	03 a	09 a	10 a	02 a	00 a
	Very little	10 a	12 b	12 a	14 a	15 b	01 a
	Somewhat	19 b	16 b	22 b	17 ab	10 b	10 b
	Most of the time	28 c	41 d	33 c	24 c	31 c	45 c
	All the time	36 d	28 c	24 b	35 d	42 d	44 c
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 5: Percentage of the obtained responses from TB patients on their subjective experiences of agitation or irritability

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long have you felt restless or irritable?	Not at all	10 a	11 a	14 a	09 a	00 a	00 a
	Very little	10 a	10 a	12 a	05 a	00 a	01 a
	Somewhat	14 a	19 ab	22 b	13 a	00 a	00 a
	Most of the time	31 b	28 c	21 b	28 b	55 b	48 b
	All the time	35 b	32 c	31 bc	45 c	45 b	51 b
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 6: Percentage of the obtained responses from TB patients on their subjective experience of encountering challenges in carrying out their routine activities

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long have you had trouble doing anything?	Not at all	18 b	15 a	10 a	11 a	09 a	08 a
	Very little	15 b	16 a	14 a	14 a	15 b	12 a
	Somewhat	10 a	22 ab	20 b	17 a	13 b	14 a
	Most of the time	26 c	18 a	30 bc	28 b	32 c	36 b
	All the time	31 c	29 c	26 b	30 b	31 c	30 b
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 7: Percentage of responses of TB patients on their experiences of discouragement and diminished capacity to restore psychological well-being

Question	Responses	2018		2019		2020	
		M	F	M	F	M	F
How long have you been so sad that nothing can cheer you up?	Not at all	05 a	02 a	07 a	03 a	00 a	00 a
	Very little	10 a	03 a	09 a	10 b	00 a	00 a
	Somewhat	24 b	15 b	19 b	22 c	00 a	01 a
	Most of the time	29 b	37 c	44 c	27 c	49 b	23 b
	All the time	32 b	43 c	21 b	38 cd	51 b	76 c
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Table 8: Responses percentage of TB patients of their experiences of feelings of worthlessness

Question	Responses	2018	2019	2020

		M	F	M	F	M	F
How long have you been feeling useless?	Not at all	25 b	26 b	19 ab	22 ab	29 c	31 b
	Very little	28 b	20 a	26 b	16 a	22 ab	24 b
	Somewhat	16 a	25 b	20 ab	24 ab	18 a	13 a
	Most of the time	12 a	12 a	15 a	18 a	14 a	16 a
	All the time	19 a	17 a	20 ab	20 ab	17 a	16 a
	Total	**100**		**100**		**100**	

Means in the same column with the same letter are not significantly different from each other at the 5% significance level

Moreover, it was observed that in the Indian population, the group affected by tuberculosis (TB) had a much higher incidence rate of depression compared to the control cohort. Specifically, the incidence rate of depression in the TB group was found to be 8.15 per 1000 person-years, whereas the control cohort had an incidence rate of 5.29 per 1000 person-years. The incidence rate is multiplied by a factor of 1.54, accompanied with a 95% confidence range ranging from 1.45 to 1.64. The findings of this study suggest that conducting stratified analyses based on gender, age group, monthly income, and comorbidities revealed a notable adjusted hazard ratio (HR) for depression among men, as well as individuals aged 65 or older, with a low monthly income and comorbidities [9].

Furthermore, a number of anti-tuberculosis medications, such as isoniazid, ciprofloxacin, ethambutol, and rifampicin, have been linked to the emergence of psychotic symptoms. The majority of existing literature has primarily examined the negative effects of isoniazid ([10]; [11]). It is worth noting that according to Holvey et al. [12], isoniazid has been identified as the second most probable medication to induce mental side effects in comparison to prednisolone, with an incidence rate of 1.9 per 100 patients. Unfortunately, there is a lack of current and publicly accessible data pertaining to the frequencies of these adverse events. The first references to this phenomenon in the scholarly literature may be traced back to 1956, when a set of three examples were documented, afterwards followed by an additional set of five cases. Following this, a number of such instances were documented. A prodromal phase, marked by symptoms such as anxiety, emotional lability, and facial twitching, was seen in a case series consisting of 38 individuals. This phase preceded the onset of psychosis. A comparable prodromal phase was identified in a cohort of 37 Polish individuals who received isoniazid treatment, all of whom had any prior mental medical records.

There have been documented instances of a murder occurring in India, whereby an incarcerated individual committed the act while experiencing a state of insanity produced by anti-tuberculosis medication. One plausible explanation for this correlation is the depletion of pyridoxine (commonly known as vitamin B6), which has been linked to the development of neuropathy. While it is advised to provide pyridoxine supplements to isoniazid patients who are at risk of developing neuropathy owing to preexisting medical disorders, there is little evidence to suggest its effectiveness in treating isoniazid-induced psychosis. According to Arya et al. [13], alternative ideas propose that isoniazid might potentially function as a monoamine oxidase inhibitor (MAOI), hence interfering with catecholamine metabolism. This mechanism of action may hypothetically induce manic psychosis in those who are already susceptible to mood disorders.

In 1999 and 2007, two further instances of psychosis produced by ethambutol were documented. Psychosis has been seen in individuals who have been administered the combination of ethionamide and isoniazid. In a single case study conducted by Martin and Bowden [14], it was shown that rifampicin has the potential to produce delirium. Moreover, there exists supporting data indicating that individuals who have psychotic symptoms while under the influence of an anti-tuberculosis therapy may also be susceptible to experiencing comparable episodes associated with other pharmaceutical substances. As an example, a particular patient had symptoms of psychosis while undergoing treatment with ethambutol, which was then terminated. However, when receiving treatment with isoniazid, the patient experienced a further episode of psychosis. Nevertheless, the patient exhibited the capacity to endure a treatment regimen including pyrazinamide, rifampicin, and ofloxacin, without manifesting any more psychotic symptoms [15].

In contrast to the TB infection itself, the use of anti-tuberculosis drugs has been linked to occurrences of suicidal conduct. Several case studies have been published documenting suicide attempts in patients who were prescribed isoniazid. Additionally, two case reports have specifically described suicide attempts that took place during a psychotic episode [16]. Furthermore, there have been case studies that have investigated a greater cohort of individuals exhibiting suicidal tendencies while being treated with isoniazid. As an example, particular research investigated six instances of Southeast Asian migrant women residing in the United States. Similarly, another study documented the occurrence of this specific side effect in eight Cambodian migrant women residing in Minnesota. Furthermore, a previous study showed the manifestation of this effect among Native Americans. In a study carried out by Sullivan et al., a total of 41 patients were examined who had sought medical attention at emergency rooms in New York City due to isoniazid poisoning. Among these patients, 27 individuals had intentionally tried suicide using this method, as reported by Blanchard et al. [17] in 1986.

A comparative analysis of suicide rates among those diagnosed with TB and those suffering from other cardio-respiratory disorders revealed a higher prevalence of suicides within the tuberculosis cohort, which may be attributed to the use of anti-tuberculosis medications. Nevertheless, a comprehensive ecological investigation conducted in 69 nations examined the relationship between population-wide

suicide rates and the occurrence and treatment rates of TB. The research, conducted by Duko et al. [18], could not identify any significant link between these variables. Cycloserine, which is administered for the management of multidrug-resistant TB, exhibits a range of mental adverse effects, with prevalence rates ranging from 20% to 33%. The substance in question functions as a substrate for D-alanine and inhibits the cell wall. Additionally, it has the ability to traverse the blood-brain barrier [19]. Psychiatric adverse effects that have been documented include symptoms such as mania, sleeplessness, and anxiety. There have been reported instances of psychosis arising as a side effect of cycloserine, with prevalence rates reaching up to 13%. Additionally, there has been documentation of a singular case involving attempted murder. Several risk factors have been discovered that are associated with an increased susceptibility to cycloserine-induced psychosis. These risks include an emotionally unstable personality, a history of drunkenness, and being female [20].

4. Conclusion

This research emphasizes the significant psychological implications of TB and antituberculosis drugs on patients, as seen by the presence of symptoms such as weariness, anxiousness, stress, and despondency, which have substantial influence on their mental health. The results underscore the need of implementing a complete approach to managing tuberculosis patients, which includes the integration of psychological support interventions. This approach aims to enhance the patients' overall well-being and promote their adherence to the prescribed treatment regimen. Furthermore, it is essential to consider gender disparities in emotional reactions towards sickness when developing support initiatives that are efficacious.

Reference

[1] Natarajan, P.M. Beena, A.V. Devnikar, and S. Mali. (2020). A systemic review on tuberculosis. Indian Journal of Tuberculosis. 67(3): 295-311.

[2] P.S. Redford, and K.D. Mayer-Barber. (2016). Tuberculosis and heterologous immunity: patterns of disease and immunity. Immunological Reviews. 264(1): 6-9.

[3] A. Pachi, D. Bratis, and G.I. Moussas. (2013). Psychiatric morbidity and other factors affecting treatment adherence in pulmonary tuberculosis patients. Tuberculosis Research and Treatment. 489865.

[4] Andries, J. Fransen, and D. Denys. (2014). Psychiatric symptoms during isoniazid therapy: prevalence and risk factors in a Belgian sample. The International Journal of Tuberculosis and Lung Disease. 18(12): 1456-1461.

[5] X. Chen, R. Wu, J. Xu, J. Wang, M. Gao, Y. Chen, and L. Zhou. (2021). Prevalence and associated factors of psychological distress in tuberculosis patients in Northeast China: a cross-sectional study. BMC Infectious Diseases. 21(1): 1-12.

[6] R.C. Kessler, G. Andrews, L.J. Colpe, E. Hiripi, D.K. Mroczek, S.L. Normand et al. (2002). Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychological Medicine. 32(6): 959–76.

[7] R.T. Brooks, J. Beard, and Z. Steel. (2006). Factor structure and interpretation of the K10. Psychological Assessment. 18(1): 62–70.

[8] H.H. Tola, D. Shojaeizadeh, G. Garmaroudi, A. Tol, M.S. Yekaninejad, L.T. Ejeta, and D. Kassa. (2015). Psychological distress and its effect on tuberculosis treatment outcomes in Ethiopia. Global Health Action. 8(1): 29019.

[9] T.C. Shen, C.Y. Wang, C.L. Lin, W.C. Liao, C.H. Chen, C.Y. and C.J. Chung. (2014). People with tuberculosis are associated with a subsequent risk of depression. European Journal of Internal Medicine. 25(10): 936-940.

[10] A. Ranjan, and S.K. Praharaj. (2014). Ciprofloxacin-induced psychosis. The Journal of Neuropsychiatry and Clinical Neurosciences. 26(1): E36-E37.

[11] A. Behera, K. Krishna, H.R. Singh. (2014). Antitubercular drug-induced violent suicide of a hospitalized patient. Case Reports. bcr2013201469.

[12] A. Holvey, A. Connolly, and D. Taylor. (2010). Psychiatric side effects of non-psychiatric drugs. British Journal of Hospital Medicine. 71(8): 432-436.

[13] S. Arya, G. Sukhija, and H. Singh. (2015). Acute psychosis after recent isoniazid initiation. Journal of Clinical and Diagnostic Research: JCDR. 9(6). VD01.

[14] S.J. Martin, and F.J. Bowden. (2007). Ethambutol toxicity manifesting as acute onset psychosis. International journal of STD & AIDS. 18(4): 287-288.

[15] Y.F. Yen, M.S. Chung, H.Y. Hu, Y.J. Lai, L.Y. Huang, Y.S. Lin, and C.Y. Deng. (2015). Association of pulmonary tuberculosis and ethambutol with incident depressive disorder: a nationwide, population-based cohort study. The Journal of clinical psychiatry. 76(4). 1539.

[16] A. Balgude, and S. Sontakke. (2012). Study of impact of antitubercular therapy on quality of life. Indian Journal of Medical Sciences. 66(3/4). 71.

[17] P.D. Blanchard, J.D. Yao, D.E. McAlpine, and R.D. Hurt. (1986). Isoniazid overdose in the Cambodian population of Olmsted County, Minnesota. Journal of American Medical Association. 256 (22): 3131-3133.

[18] Duko, A. Bedaso, and G. Ayano. (2020). The prevalence of depression among patients with tuberculosis: a systematic review and meta-analysis. Annals of General Psychiatry. 19(1): 1-11.

[19] J.S. Kass, and W.X. Shandera. (2010). Nervous system effects of antituberculosis therapy. CNS Drugs. 24: 655-667.

[20] P.C. Bürkner, N. Bittner, H. Holling, and U. Buhlmann. (2017). D-cycloserine augmentation of behavior therapy for anxiety and obsessive-compulsive disorders: A meta-analysis. PloS One. 12(3): e0173660.